Complete Summary

GUIDELINE TITLE

Breast cancer.

BIBLIOGRAPHIC SOURCE(S)

Breast cancer. Philadelphia (PA): Intracorp; 2005. Various p. [41 references]

GUIDELINE STATUS

This is the current release of the guideline.

All Intracorp guidelines are reviewed annually and updated as necessary, but no less frequently than every 2 years. This guideline is effective from April 1, 2005 to April 1, 2007.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

On August 31, 2005, Genentech and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of updated cardiotoxicity information related to the use of Herceptin (trastuzumab), obtained from the National Surgical Adjuvant Breast and Bowel Project (NSABP) study (B-31), a randomized, Phase III trial that was conducted in 2043 women with operable, HER2 overexpressing breast cancer (IHC 3+ or FISH+). This study demonstrated a significant increase in cardiotoxicity in patients who were randomized to the Herceptin-containing arm as compared to patients who received chemotherapy alone. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Breast cancer, including

- Adenocarcinoma (ductal or lobular) in situ
- Invasive ductal or lobular carcinoma
- Inflammatory breast cancer
- Medullary carcinoma
- Mucinous carcinoma
- Tubular carcinoma
- Phyllodes tumor
- Paget's disease of the nipple

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Oncology
Surgery

INTENDED USERS

Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Utilization Management

GUIDELINE OBJECTIVE(S)

To present recommendations for the diagnosis, treatment, and management of breast cancer that will assist medical management leaders to make appropriate benefit coverage determinations

TARGET POPULATION

Individuals with breast cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Physical examination and assessment of signs and symptoms
2. Diagnostic tests:
    - Mammography
    - Clinical and self-breast examination
    - Ultrasound
    - Ductogram
    - Biopsy (excisional, fine needle aspiration)
    - Radionuclide bone scan, if indicated
    - Magnetic resonance imaging (MRI)
    - Blood studies for surgical clearance
    - Genetic testing in high-risk individuals
    - Proto-oncogen HER-2 assessment
    - HercepTest® or routine immunohistochemistry

Treatment/Management/Prevention

1. Medical therapy
    - Hormone replacement therapy
    - Chemotherapy
    - Tamoxifen (Nolvadex®)
    - Trastuzumab (Herceptin®)
2. Radiation therapy
3. Surgery
    - Lumpectomy
    - Mastectomy (partial, modified radical, or radical)
    - Bilateral prophylactic mastectomy
    - Reconstructive surgery
4. Physical therapy
5. Referral to specialists
6. Case management strategies, including case initiation, case management focus, and discharge

Note: Sentinel lymph node biopsy is believed very accurate but is still under investigation.

MAJOR OUTCOMES CONSIDERED

- Risk factors for breast cancer
- Incidence of breast cancer
- Risks and side effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches were performed of the following resources: reviews by independent medical technology assessment vendors (such as the Cochrane Library, HAYES); PubMed; MD Consult; the Centers for Disease Control and Prevention (CDC); the U.S. Food and Drug Administration (FDA); professional society position statements and recommended guidelines; peer reviewed medical and technology publications and journals; medical journals by specialty; National Library of Medicine; Agency for Healthcare Research and Quality; Centers for Medicare and Medicaid Services; and Federal and State Jurisdictional mandates.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A draft Clinical Resource Tool (CRT or guideline) is prepared by a primary researcher and presented to the Medical Technology Assessment Committee or the Intracorp Guideline Quality Committee, dependent upon guideline product type.

The Medical Technology Assessment Committee is the governing body for the assessment of emerging and evolving technology. This Committee is comprised of

a Medical Technology Assessment Medical Director, the Benefit and Coverage Medical Director, CIGNA Pharmacy, physicians from across the enterprise, the Clinical Resource Unit staff, Legal Department, Operations, and Quality. The Intracorp Guideline Quality Committee is similarly staffed by Senior and Associate Disability Medical Directors.

Revisions are suggested and considered. A vote is taken for acceptance or denial of the CRT.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The guideline developers reviewed a published cost analysis.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Diagnostic Confirmation

Subjective Findings

- Breast mass(es)
- Breast pain or tenderness
- Weight loss (in advanced disease)
- Bone pain (in metastatic disease)

Objective Findings

- Asymmetry of breasts
- Tenderness
- Induration
- Hard, circumscribed mass in the breast, may be fixed to the skin or chest wall
- Nipple retraction, inversion, and/or discharge
- Skin changes, such as dimpling and peau d'orange ("orange peel") appearance
- Localized edema
- Localized erythema

Diagnostic Tests

- Mammography (breast radiography), standard primary test (see the Intracorp guideline Imaging: Breast for approval criteria)
    - American Cancer Society (ACS) recommends for women age 40 and greater to have a mammography, clinical breast exam (CBE) annually. This should be continued for as long as good health indicates a woman would be a candidate for treatment
    - For women in their 20s and 30s, ACS recommends a periodic CBE by a health professional preferably every 3 years
    - Self-Breast Examination (SBE): optional for women age 20 and older according to latest ACS protocol (refer to ACS Web address http://www.cancer.org/docroot/NWS/content/NWS_1_1x_Role_Of_Breast_Self-Examination_Changes_In_Guidelines.asp)
    - Women at increased risk should review the benefits and limitations of starting mammograms before age 40, having additional tests, and/or having more frequent CBEs.
- Ultrasound (US) - used to resolve equivocal mammography findings, especially in dense breasts (see the Intracorp guideline Imaging: Breast)
- Ductogram (or galactogram) - may be helpful in determining cause of nipple discharge
- Excisional biopsy - diagnostic "gold standard"; surgical removal of an entire lesion (see the Intracorp guideline Lumpectomy)
- Sentinel lymph node biopsy, believed to be very accurate but still under investigation
- Fine needle aspiration biopsy (FNA/B) - to diagnose cysts and to provide treatment (see the Intracorp guideline Breast Biopsy)
    - May be performed in conjunction with US to help localize tiny lesion (stereotactic needle biopsy)
- Radionuclide bone scan indicated only for patients with documented breast cancer who have bone pain
- Magnetic resonance imaging (MRI) for cancer identification/staging (see the Intracorp guideline Imaging: Breast)
- Blood studies as indicated for surgical clearance
- Genetic testing ("genotyping") indicated ONLY in individuals at high risk established by congenital tendencies for breast cancer inheritance; should be performed along with appropriate pre- and post-test genetic counseling
    - Medical necessity for BRCA-1 and BRCA-2 susceptibility screening (adapted from the National Comprehensive Cancer Network Clinical Practice Guidelines on Genetic/Familial High-Risk Assessment: Breast and Ovarian, Version 1.2004):

1. Patients with no personal history of breast cancer who have a first- or second-degree relative with a known BRCA1 or BRCA2 mutation
2. Patients with a personal history of breast cancer when at least one of the following is met:
    - Cancer was diagnosed at age 40 or younger, regardless of family history
    - Cancer was diagnosed at age 50 or younger, with at least one first- or second-degree relative with breast cancer at age 50 or younger
    - Cancer was diagnosed at age 50 or younger, with at least one first- or second-degree relative with ovarian cancer

- Cancer was diagnosed as bilateral, with at least one first- or second-degree relative with breast cancer at age 50 or younger
- Cancer was diagnosed as bilateral, with at least one first- or second-degree relative with ovarian cancer
- Cancer was diagnosed at any age, with at least two first- or second-degree relatives with ovarian cancer at any age
- Cancer was diagnosed at any age, with at least two first- or second-degree relatives with breast cancer, especially if at least one woman is diagnosed before age 50 or has bilateral breast cancer the patient also has a personal history of ovarian cancer
- The patient is of Ashkenazi Jewish descent and breast cancer was diagnosed at age 50 or younger
- The patient is of Ashkenazi Jewish descent, when there is a history of breast and/or ovarian cancer in a first- or second-degree relative

3. Patients with a personal history of ovarian cancer when at least one of the following is met:
    - Patient has at least one first- or second-degree relative with ovarian cancer
    - Patient has at least one first- or second-degree female relative with breast cancer diagnosed at age 50 or younger
    - Patient has at least one first- or second-degree female relative with bilateral breast cancer
    - Patient has at least two first- or second-degree relatives with breast cancer
    - Patient has at least one first- or second-degree male relative with breast cancer
    - If the patient is of Ashkenazi Jewish descent, no additional family history is required
4. Male patients with a personal history of breast cancer when at least one of the following is met:
    - Patient has at least one first- or second-degree relative with breast cancer
    - Patient has at least one first- or second-degree female relative with breast or ovarian cancer
    - Patient is of Ashkenazi Jewish descent, no additional family history is required
5. Patients without a personal history of cancer (unaffected individuals) who have a first- or second-degree relative or who meet any of the above criteria
    - The proto-oncogene HER-2, is known to be overexpressed, amplified, or both in 20% to 30% of breast cancers
    - There are various methods to assess HER-2 deoxyribonucleic acid (DNA) amplification status in breast cancer: protein over-expression as determined by standard immunohistochemistry (IHC) methods, and gene amplification using fluorescence in situ hybridization (FISH) method are most commonly utilized
    - Most importantly, (+) HER-2 status is predictive for response to therapy with trastuzumab (Herceptin®)
    - HercepTest® (DakoCytomation, Denmark), approved September 1998 by the U.S. Food and Drug Administration (FDA), may be used to identify those patients with advanced breast cancer and metastasis who may benefit from treatment with trastuzumab

- Routine immunohistochemistry using the DAKO A0485 antibody is a reliable, cost-effective alternative to the HercepTest in determining prognosis and suitability of patients for trastuzumab therapy

Differential Diagnosis

- Fibrocystic disease
- Fibroadenoma
- Papilloma
- Mastitis
- Abscess
- Fat necrosis
- Paget's disease of the breast
- Gynecomastia

Treatment Options

- Hormone replacement therapy (carries risk of associated deep venous thrombosis, ovarian cancer, as well as breast cancer)
    - Self-administered
- Chemotherapy, performed in single or repeating cycles (see the Intracorp guideline Chemotherapy)
    - Care Setting:
        - Primarily clinic or free-standing outpatient, physician's office, or home care
        - Possibly acute inpatient, subacute/skilled nursing facility inpatient, or hospice inpatient if activities of daily living (ADL) severely compromised
- Tamoxifen (Nolvadex®), approved by FDA
    - Effective in reducing the incidence/primary prevention of breast cancer in high-risk women
    - Also useful as an adjuvant therapy to primary treatment for early stage breast cancer
    - Estrogen antagonist, antineoplastic
    - Women with slightly increased breast cancer risk probably do not gain significant benefits in consideration of risks associated with tamoxifen (increased incidence of endometrial cancer, pulmonary and cerebrovascular emboli, and cataracts)
    - Women at highest risk may receive little preventive benefit
    - No clear recommendation can be given regarding what constitutes a high-risk group of women for whom tamoxifen is appropriate as a breast cancer preventive agent
        - Care Setting: refer to Chemotherapy, above
- Biological response modifier therapy, Trastuzumab (Herceptin®), approved by FDA for treatment in:
    - Advanced breast cancer or cancer spread beyond breast and lymph nodes
    - Certain patients with history of failed, one-time trial of chemotherapy
    - Metastatic disease, first-line treatment when used in combination with Paclitaxel (Taxol®)
        - Care Setting: refer to Chemotherapy, above
- Radiation therapy, performed in single or repeated series of sessions

        - Care Setting: refer to Chemotherapy, above
- Surgical options
    - Lumpectomy - removal of the lump or tumor and a small amount of breast tissue around it, leaving the rest of the breast intact. Preferred procedure when cancer is contained (see the Intracorp guideline Lumpectomy)
    - Wide local excision with radiation, partial mastectomy or lumpectomy with adjuvant radiation therapy - according to the American Cancer Society (ACS), long-term survival rates after lumpectomy plus radiotherapy are similar to those after modified radical mastectomy (early-disease studies)
        - Care Setting: acute inpatient (see the Intracorp guideline Lumpectomy)
    - Modified radical mastectomy, surgical removal of breast along with lymph node dissection
        - Care Setting: acute inpatient
    - Radical mastectomy - surgical removal of breast and adjacent pectoralis muscle tissue, rarely used
        - Care Setting: acute inpatient (see the Intracorp guideline Mastectomy)
    - Sentinel node biopsy, emerging technique for disease staging by locating and exploring most prominent lymph node, believed very accurate but continuing to be evaluated.
        - Care Setting: outpatient or free-standing clinic, physician's office; acute inpatient facility if patient severely deconditioned
    - Bilateral prophylactic mastectomy - reduces breast cancer incidence in women with high risk based on family history
        - Care Setting: acute inpatient; generally expect short stay and good outcome as surgery performed when no overt disease manifested
    - Reconstructive surgery - done at the time of the mastectomy (immediate reconstruction) or at some subsequent time (delayed reconstruction) to restore an approximation of pre-operative anatomical appearance
        - Care Setting: acute inpatient

Duration of Medical Treatment

- Medical - Optimal: 7 day(s), Maximal: 70 day(s)
    - Duration of treatment varies with many factors, including cancer stage and histologic type, original tumor size, number and location of involved lymph nodes, and hormone or chemotherapy responsiveness.
        - Need for surgical versus non-surgical treatment
        - Decision for reconstruction after mastectomy

Additional information regarding primary care visit schedules, referral options, specialty care, physical therapy, and durable medical equipment is provided in the original guideline document.

The original guideline document also provides a list of red flags that may affect disability duration, and return to work goals, including

- After lumpectomy with radiation
- After mastectomy
- During chemotherapy
- In confirmed metastatic disease

Note: Some patients with this condition may never return to work.

Case Management Directives (refer to the original guideline for detailed recommendations)

Case Initiation

Establish Case

- Document baseline information, history, key physical findings, patient's understanding, and safety factors.
- See Chemotherapy Chart in the original guideline document.
- The American Joint Committee on Cancer encourages use of the "TNM" classification system (T=primary tumor size; N=lymph node involvement; M=metastasis).
- Provide contact information for local and national support groups.

Coordinate Care

- Advocate for patient by managing utilization and charges.
- Document treatment plan.

Case Management Focus

Activity Deficit

- Document activity alteration as none, mild, moderate, severe, dependent, or bed-bound (based on most recent performance status) and interventions required.

Chemotherapy Intolerance

- Assess status, acute versus chronic, of toxic side effects on rapidly growing tissues, including bone marrow, epithelium, hair, sperm, and document intervention recommended.

Hemodynamic Instability

- Document bleeding complications, severity, and intervention recommended.

Immune Compromised

- Document establishment of protective isolation measures for a white blood cell count (WBC) less than 1,000/mm^3, implying dangerous susceptibly to infection.

Inadequate Nutrition

- Recommend to women who report painful breasts to refrain from caffeine consumption (e.g., chocolate, coffee, cola, and tea) and to modify salt intake for 5 to 7 days prior to mammography.
- Use optimal goal of remaining within 10% of pretreatment weight to document hydration and nutrition deficit as mild, moderate, severe and response needed.

Mental and Emotional Alteration

- Ensure accurate diagnosis of any change in mental status.
- Document baseline or optimal mental and emotional functioning and their alterations due to cancer presence, comorbidity, surgery, or treatments.
- Assess and respond appropriately to the degree of debility caused by alterations listed in the original guideline document through benefit coordination or community resource activation.

Pain Control

- Recommend for discomfort caused by breast tissue inflammations, infection, or shooting pains the use of adequate rest and hydration, careful personal hygiene, decrease salt and caffeine intake, local heat, snug supportive bra.
- Assess the need for diuretics, analgesics, or oral contraceptives for persistent pain.
- Document optimal pain management by characterizing severity and interventions undertaken to remedy or manage pain.

Oncologic Emergencies

- Document presence of or developing oncologic emergencies and report to attending physician, surgeon, or activate emergency medical technician (EMT) system as necessary.

Radiation Intolerance

- Document presence and severity of radiation side effects.
- Initiate early interventions for complications of radiation therapy.

Respiratory Instability

- Document respiratory deficit as mild, moderate, severe, and dependent, and respiratory rehabilitation enhancement measures.

Skin Integrity Deficit

- Refer immediately under conditions of breast discharge (non-lactation), marked ulceration, unrelieved pain, or recurring fissures to the attending physician or specialist.
- Advise concerned patients cyst size may fluctuate with menstrual cycle (larger, during premenstrual phase; smaller, postmenstrual).

- Instruct that fissures (longitudinal ulcerated areas) may develop while breast-feeding.
- Document severity of skin integrity disruption.

Terminal Care

- Document optimal comfort measures and palliative care initiatives.

Discharge

Discharge from Case Management (CM)

- Document return to independence or stabilized functional status and closing conversations with patient, caregiver, physician, pharmacist, and care providers.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall Potential Benefits

Appropriate diagnosis, treatment, and management of breast cancer that assist medical management leaders in making appropriate benefit coverage determinations

Specific Potential Benefits

- Tamoxifen (Nolvadex®) is effective in reducing the incidence/primary prevention of breast cancer in high-risk women.
- Bilateral prophylactic mastectomy reduces breast cancer incidence in women with high risk based on family history.

POTENTIAL HARMS

Refer to the Case Management Focus section of the "Major Recommendations" field for information on potential complications and strategies to address them, or refer to the original guideline document.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Breast cancer. Philadelphia (PA): Intracorp; 2005. Various p. [41 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1997 (revised 2005)

GUIDELINE DEVELOPER(S)

Intracorp - Public For Profit Organization

SOURCE(S) OF FUNDING

Intracorp

GUIDELINE COMMITTEE

CIGNA Clinical Resources Unit (CRU)
Intracorp Disability Clinical Advisory Team (DCAT)
Medical Technology Assessment Committee (MTAC)
Intracorp Guideline Quality Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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GUIDELINE AVAILABILITY

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Reprints of complete guideline content may be purchased for $35.00 per title (plus tax in TX at 8.25% and CT at 1.0%). Please send e-mail request to lbowman@mail.intracorp.com.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Policies and procedures. Medical Technology Assessment Committee Review Process. Philadelphia (PA): Intracorp; 2004. 4 p.
- Online guideline user trial. Register for Claims Toolbox access at www.intracorp.com.

Licensing information and pricing: Available from Intracorp, 1601 Chestnut Street, TL-09C, Philadelphia, PA 19192; e-mail: lbowman@mail.intracorp.com.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 24, 2005. The information was verified by the guideline developer on June 7, 2005. This summary was updated by ECRI on September 8, 2005 following the U.S. Food and Drug Administration (FDA) advisory on Herceptin (trastuzumab).

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Date Modified: 5/22/2006